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51. (New) The nucleic acid of claim 48, wherein the target polypeptide interaction domain is selected from the group consisting of a papillomavirus E7 polypeptide, and an SV40 LTP polypeptide.

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52. (New) A hybrid-polypeptide for use in degrading a target polypeptide comprising an F-box polypeptide that is functionally linked to a target polypeptide interaction domain.

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53. (New) The hybrid-polypeptide of claim 52, wherein the F-box polypeptide sequence is selected from the group consisting of SEQ ID Nos. 2, 4, 6, 8, 10 and 12.

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54. (New) The hybrid-polypeptide of claim 52, wherein the target polypeptide interaction domain is selected from the group consisting of a papillomavirus E7 polypeptide, and an SV40 LTP polypeptide.

#### REMARKS

The entering of new claims 36-54 create no new matter. Support for the new claims can be found throughout the application, for example, in original claims 1-35, at page 178-181, as well as in the specification at pages 8-10. The above amendments have been made in an effort to expedite prosecution of the application, and not in acquiescence to any of the Examiner's rejections. Applicants expressly reserve the right to pursue without prejudice the originally filed claims as well as other disclosed subject matter at a latter date.

Applicants note that the Final Office Action dated March 27, 2002 states that claims 1-4, 6-11, 14 and 15 are pending and under consideration. In response to the Final Office Action, Applicants have: (1) conducted an interview with the Examiner on July 2, 2002 - for which Applicants are grateful; and (2) filed this Preliminary Amendment and Response in conjunction with a Request for Continued Examination pursuant to 37 C.F.R. § 114, in which they have canceled pending claims 1-4, 6-11, 14 and 15 and added new claims 36-54. The rejections set forth in the Final Office Action are addressed below in the order in which they are raised by the Examiner.

## REJECTIONS

### Rejections Under 35 U.S.C. §112, first paragraph-Written Description

The Office Action states that claims 1-4, 6-11, 14 and 15 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the Final Office Action dated March 27, 2002 states that “the hybrid protein suitable for use in a claimed method is described by broad function.” Applicants respectfully traverse this rejection. Applicants believe entry of new claim 36-54 obviate this rejection. There is ample support in the application for the F-box methods and compositions specifically claimed. Furthermore, the skilled artisan, at the time of the invention, was aware of further support for the F-box structures that are a part of the claimed invention (see, for example, F-box domain descriptions including F-Box, CD: pfam00646 at [www.ncbi.nlm.nih.gov/Structure](http://www.ncbi.nlm.nih.gov/Structure)). Accordingly, Applicants believe new claims 36-54 are defined in structural terms that are well supported in the application and also well known in the art to the skilled artisan at the time of the invention and consideration and allowance is respectfully requested.

### Rejections Under 35 U.S.C. §112, first paragraph-Enablement

The Office Action states that claims 1-11(sic), 14 and 15 have been rejected under 35 U.S.C. § 112, first paragraph, as “not reasonably provid(ing) enablement for a method of use of any hybrid based on any component of ubiquitin ligase.” In particular, the Final Office Action dated March 27, 2002 states that “the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims.” Applicants respectfully traverse this rejection. Applicants believe entry of new claim 36-54 obviate this rejection. There is ample support for making and using the F-box methods and compositions specifically claimed. In particular, Applicants believe new claims 36-54 are defined in sufficiently specific structural terms that the skilled artisan at the time of the invention, using only the teachings of the invention, could readily make and use the F-box methods and compositions commensurate with these new claims. Accordingly, prompt consideration and allowance of new claims 36-54 is respectfully requested.

## CONCLUSION

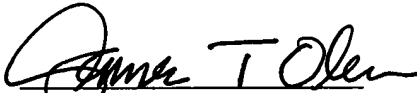
For the foregoing reasons, Applicants respectfully request entry of new claim 36-54 and prompt consideration and withdrawal of the previous rejections. Applicants believe that the claims now pending are in condition for allowance, and notification of such is respectfully requested. If for any reason a telephonic conference with the Applicant would be helpful in expediting prosecution of the instant application, the Examiner is invited to call Applicants' Agent at (617) 832-1764.

If there are any other fees due in connection with the filing of this Response, please charge the fees to our Deposit Account No. 06-1448.

Respectfully submitted,  
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